REMARKS

Applicants have amended claims 1 and 18 to make explicit that which was implicit, namely that the microchannels are designed to use their shape as a geometric constraint to trap or capture a cell as it traverses the microchannel, causing the cell's progress through the microchannel to be halted. This amendment is supported at lines 1-2 of page 6 and does not introduce new matter; their entry is respectfully requested. Claim 2 has been amended to further define the design of the gradient array. This amendment is supported at page 6, lines 1-16, as well as Figure 2, and does not introduce new matter. Its entry is respectfully requested. Claim 4 has been amended to remove the term "substantially" to clarify what is being claimed. This amendment is supported at pages 7-8 of the specification, as well as Figure 3B. This amendment does not introduce new matter and its entry is respectfully requested. Claim 18 has further been amended to correct an informality (i.e. adding "wherein"), this amendment is supported by the original claim. Entry of the above amendments is respectfully requested.

Applicants appreciate the Examiner's withdrawal of the rejection of the claims under 35 U.S.C. § 112, second paragraph.

Claims 1- 18 were rejected under 35 U.S.C. § 102(b) as being anticipated by Sutton et al.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

The present invention is directed to a human erythrocyte microchannel analyzer, or HEMA, which enables morphological measurements of a large number of individual cells to be rapidly determined. Previous technologies allowed measurements of either a *population* of red blood cells, but not the properties of individual cells within the population, or measurements of *individual* cells, which could not be collected in large numbers. As described in the article submitted with the prior response, describing the present invention, the HEMA of the present invention now allows analysis of 500 *individual* cells in five minutes (see page 3, first full paragraph). Morphological properties which can be measured using HEMA include cell surface area, cell volume, and

deformability of individual cells. In this device, red blood cells are trapped for analysis in microfabricated channels, which are designed to trap or capture the cells. In several preferred embodiments, the HEMA uses the position of the cell after it has come to rest in a specific location, in other words it takes a <u>static measurement</u>.

In contrast, the microchannel instrument of Sutton is designed to measure the velocity of a cell <u>as it moves through a microchannel</u>. As described in the Sutton Abstract, the "instrument characterizes each cell in a sample of ca. 1000 in terms of its volume and <u>flow velocity profile during its transit through a channel</u>" [emphasis added]. The Sutton microarray is necessarily limited to the measuring the <u>transit</u> of cells through microchannels, and is not designed to <u>capture</u> cells, as required by the claim 1.

The Examiner has contended that the Sutton instrument "captures" cells simply because these cells are "contained within the microchannel" (June 8, 2004 Office Action, page 4, line 16). However, the Examiner explicitly acknowledges that the cells in the Sutton instrument "are **flowing** through the channel array" (Office Action, page 4, line 15; emphasis added).

Applicants respectfully submit that the amendment to claim 1 has obviated this claim, by making explicit that which was implicit, namely that the shape of the microchannel is designed to be a geometric constraint to trap a cell as it traverses the microchannel, such that the trapped cell does not leave the microchannel but is constrained by its shape to remain in the microchannel. Thus, it is clear that the array of claim 1 captures cells such that they are

The Examiner has also contended that the term "gradient" in claim 2 cannot be interpreted to mean a gradient array, because it is not defined in the specification, nor is its meaning clear from claim 2. Applicants have now amended claim 2 to make explicit that the claim is directed to the gradient array of the present invention. More particularly, the array is now clearly recited to be a gradient array, with microchannels designed to have certain specific structure and arrangements to create a gradient array.

Moreover, the gradient array of the present invention is patentably distinguishable over Sutton, because while the Sutton instrument includes microchannels of different widths on a single array (see e.g. Figure 1), these channels are not arranged to form a gradient, for example, see one embodiment depicted in Figure 2 of the present invention. The present invention provides many

variations of sequential channels. For example, the gradient array depicted in Figure 2 has a series of increasingly smaller channels. The Examiner seems to suggest that applicants cannot rely on the Figures to define elements of the claims; however, applicants respectfully submit that they are entitled to rely on all parts of the entire disclosure, including the drawings, in defining the invention. As described above, as well as at page 6, paragraphs 2 – 4 of the specification, the gradient array is specifically taught as being designed to "trap" or capture the red blood cells. The Sutton array of single, parallel channels through which cells flow is not designed to allow the cells to enter multiple channels sequentially, nor is it designed to trap the cells, as required by the gradient array of claim 2 of the present invention. Sutton Figures 1, 3, 4, and 5 all clearly indicate that the instrument comprises a series of parallel channels, each with a single entry point and a single exit point, such that once a cell enters a channel, its eventual fate will be to emerge from the opposite end of the channel without the opportunity to enter a second microchannel, as it has exited the channel array. Accordingly, Sutton further does not anticipate the claims, because claim 2 specifically recites that it is directed to a gradient array of microchannels, and the Sutton does not comprise a *gradient* of microchannels.

The Examiner has also taken the position that Sutton teaches the use of "substantially wedge-shaped" channels as recited in claim 4. The Examiner has argued that because the "wedge-shaped" is not defined in the specification, nor is there an indication that "wedge-shaped" as recited in claim 4 should be interpreted to mean the wedge shape depicted in Figure 3B, that the microchannels of the present array are not distinguishable from the Sutton microchannels.

Applicants respectfully disagree for the following reasons. First and foremost, applicants respectfully submit that the terms "substantially," "wedge-shaped," and thus "substantially wedge-shaped" are all terms with plain meaning, which are well understood by most people. For example, Webster's 1913 Dictionary supplies the following definitions:

> 1. Having the shape of a wedge; cuneiform.
> 2. (Bot.) Broad and truncate at the summit, and tapering down to the base; as, a wedge-shaped leaf.

Thus, it is plain that the shape of a microchannel may be understood to be a channel in three dimensions, which is described as "wedge-shaped," and has one broad end of the channel, which

tapers down to the other end (i.e. the base). Indeed, this is exactly the general shape depicted in Figure 3B, and described in detail on page 7, lines 16 – 19, the wedge shaped channels of the present invention vary their dimensions within a single channel. This wedge shape is depicted in Figure 3B. Applicants have amended claim 4 to remove the phrase "substantially," to further clarify that what is being claimed is a wedge-shaped microchannel.

In contrast, the different microchannels of Sutton have differing dimensions, but nothing Sutton teaches or suggests that a single channel should be wedge-shaped. Indeed, page 278, column 1 describes that the instrument has "a repeated group of six different channels, each having a constant width between 3.0 and 4.0 μm with channel width increments of 0.2 μm" (page 278, col. 1, lines 15 – 18) – not a wedge-shape. While the width of different channels varies in the Sutton instrument, each individual channel has a constant width and thus is not wedge-shaped. The wedge-shaped channels of the present invention would in fact work against the functioning of the Sutton instrument, because they do not permit the cell's transit through the entire channel, but rather, are designed to capture or trap the cells.

Accordingly, applicants respectfully submit that these rejections of the claims should be withdrawn.

Claims 1 – 18 were rejected under 35 U.S.C. § 102(b) as being anticipated by Brody.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

Like Sutton, Brody is directed to the real-time analysis of red blood cells during their transit through microchannels. The title and abstract clearly indicate that Brody looks at cells "flowing through the bed at physiological speeds" (Abstract). Like Sutton, Brody uses video microscopy to track the movement of single cells through the array. Figures 2, 5, 8, and 9 of Brody all show images of cells moving through an array. Thus, the function of the Brody array is again entirely dependent upon the continued flow of the cells through the microchannels. In contrast, claim 1 of the present invention requires the microchannel to capture the cell, blocking its further movement through the array.

In issuing this rejection, the Examiner has essentially repeated the arguments made in rejecting the claims over Sutton, namely, that the phrases "capturing," "gradient," and "substantially

wedge-shaped" all render the claims anticipated by the Brody instrument. Applicants respectfully submit that for all of the reasons outlined above with respect to Sutton, including all of the amendments to the claims, Brody does not anticipate the claims of the present invention. For example, Brody does not teach wedge-shaped channels. Similarly, the Brody array does not teach a configuration of a gradient of microchannels of decreasing width, designed to capture the red blood cell and block its further movement through the array. Accordingly, applicants respectfully submit that these rejections of the claims should be withdrawn.

Accordingly, in view of the foregoing, applicants respectfully submit that all claims comply with 35 U.S.C. § 102(b).

In view of the foregoing, applicants submit that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our deposit account No. 50-0850.

Respectfully submitted,

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